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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,142	02/15/2002	Robert John D'Amato	05213-3000 (43170-269288)	2351
23370	7590	06/15/2004	EXAMINER	
JOHN S. PRATT, ESQ KILPATRICK STOCKTON, LLP 1100 PEACHTREE STREET SUITE 2800 ATLANTA, GA 30309			BADIO, BARBARA P	
			ART UNIT	PAPER NUMBER
			1616	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/077,142

Applicant(s)

D'AMATO ET AL.

Examiner

Barbara P. Badio, Ph.D.

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-41 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 30-41 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 122003:022004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

Final Office Action on the Merits

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. **The rejections of claim 29 under 35 USC 112, first paragraph is made moot by the cancellation of the instant claim.**

3. The rejections of claims 30-40 under 35 USC 112, first paragraph is maintained and claim 41 is rejected under 35 USC 112, first paragraphs.

Applicant argues that all neovascularization in human or animal is associated with angiogenesis and, thus, the term neovascularization is not broader than angiogenesis. Applicant's argument was considered but not persuasive for the following reasons.

First, if according to applicant, neovascularization is equivalent to angiogenesis, it is suggested the term "angiogenesis" be used in the instant claims. Said substitution would overcome the present rejection.

Angiogenesis is a mechanism of neovascularization that involves the development of blood vessels from pre-existing capillaries. Neovascularization includes the processes of angiogenesis, arteriogenesis and vasculogenesis (see the attached articles, US 5,015,629, col. 1, lines 41-44; Franco, US 2002/0058612, see section 0005; Herron, US 2003/0175961, see sections 0103 and 0105; Simons, General concepts of

Art Unit: 1616

angiogenesis and Benedict et al., Annals of Internal Medicine, see Figure 1). Thus, based on the art, neovascularization would be broader than angiogenesis.

For these reasons and those given in previous Office Action, the rejections of claims 30-40 under 35 USC 112, first paragraph is maintained and claim 41 is rejected under 35 USC 112, first paragraphs.

Double Patenting

4. The provisional rejection of claim 29 under the judicially created doctrine of obviousness-type double patenting over claims of copending Application No. 10/280,831 is made moot by the cancellation of the instant claim.

5. The provisional rejection of claims 30, 32, 33, 35, 36, 38 and 39 under the judicially created doctrine of obviousness-type double patenting over claims of copending Application No. 10/280,831 is maintained and claim 41 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims of copending Application No. 10/280,831.

Applicant notes that no response is required at this time because the rejection is a provisional rejection.

6. The provisional rejection of claim 29 under the judicially created doctrine of obviousness-type double patenting over claims of copending Application No. 10/080,076 is made moot by the cancellation of the instant claim.

7. The provisional rejection of claims 30-40 under the judicially created doctrine of obviousness-type double patenting over claims of copending Application No. 10/080,076 is withdrawn.

It is noted that the patented subject matter does not read on the instant claims (see US Patent No. 6,723,858).

8. The rejections of claim 29 under the judicially created doctrine of obviousness-type double patenting over claims of US Patent Nos. 5,504,074 and 5,661,143 are made moot by the cancellation of the instant claim.

9. The rejections of claims 30-40 under the judicially created doctrine of obviousness-type double patenting over claims of US Patent Nos. 5,504,074 and 5,661,143 are maintained and claim 41 is rejected under the judicially created doctrine of obviousness-type double patenting over claims of US Patent Nos. 5,504,074 and 5,661,143.

It is noted that the terminal disclaimer referred to by applicant is not of record in the present application.

Claim Rejections - 35 USC § 102

10. The rejection of claim 29 under 35 USC 102(b) over Seegers et al. is made moot by the cancellation of the instant claim.

11. The rejection of claims 30, 35 and 36 under 35 USC 102(b) over Seegers et al. is maintained and claim 41 is rejected under 35 USC 102(b) over Seegers et al.

Applicant's argument is that the reference discloses 2-methoxyestradiol is anti-mitotic and suggests that it "may be the ultimate cytotoxic compound". According to applicant, a useful therapeutic agent is one that is selectively toxic to abnormal cells, but minimally toxic to normal cells and it was only after realizing 2-methoxyestradiol had anti-microtubule activity could applicants conclude the compound could be useful for treatment of neovascularization. Applicant also argues the reference fails to disclose a single disease that is treatable with 2-methoxyestradiol. Applicant's argument was considered but not persuasive for the following reasons.

Applicant argues the reference is teaching the compound is toxic and, thus, would be considered by the skilled artisan as nothing more than an "indiscriminant poison". The examiner disagrees with applicant's interpretation of the teachings of the Seegers. There are several references made by Seegers that would imply the toxic effect discussed is that of the action of the compound on abnormal cells and not normal cells. For example, (a) on page 801, col. 2, the reference discloses "high levels (1×10^{-6} M) of the steroids had little stimulating effect on normal metaphase formation during the 24 h exposure period in MCF-7 cells" and "there was, however, a marked stimulating effect on abnormal metaphase formation"; (b) on page 802, col. 2, the reference states "normal metaphase formation was not affected by any of the methoxy metabolites at high concentration levels (Fig. 10)"; (c) on page 803, col. 1, Seegers also states "the 2-MeOE₂ caused marked increases in the number of abnormal metaphases

(Fig. 11)" and (d) on page 808, col. 2, it is stated that of all the estrogens studied in the experiments "2-MeOE₂ holds the greatest potential as an antitumour agent, because of its toxic effects on dividing malignant MCF-7 and HeLa cells". Thus, the skilled artisan would not consider the compound an indiscriminant poison as suggested by applicant but would realize that 2-methoxyestradiol is only toxic to abnormal cells.

In response to applicant's argument that the reference does not disclose a single disease that is treatable by 2-methoxyestradiol, it is noted that the claimed invention is to a method of inhibiting neovascularization and not to the treatment of any disease.

For these reasons and those given in previous Office Action, the rejection of claims 30, 35 and 36 under 35 USC 102(b) over Seegers et al. is maintained and claim 41 is rejected under 35 USC 102(b) over Seegers et al.

Claim Rejections - 35 USC § 103

12. The rejection of claims 31-34 and 37-40 under 35 USC 103(a) over Seegers et al. is maintained.

Applicant's argument and the examiner's response are as discussed above in #11.

Other Matters

13. Applicant's information disclosure statement filed May 14, 2004 will be considered when it becomes available to the examiner.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

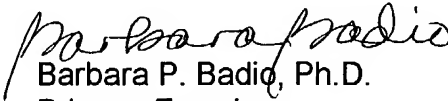
Telephone Inquiry

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1616

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1616

BB

June 9, 2004